Advances in Bioresearch
Adv. Biores., Special Issue (3) 2025: 59-63

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585. SPL3.25.5963

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Efficacy of Drugs in Management of Pancreatic Pain in Chronic Pancreatitis

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ABSTRACT

Chronic pancreatitis (CP) is inflammation of pancreas causing intense abdominal pain. Management of pain involves gradual increase in potency of analgesic drugs until the discomfort subsides. Aim of study was to evaluate the efficacy of drugs in pain management in chronic pancreatitis and to assess severity of pain before and after treatment. A prospective, cross-sectional study was conducted for a period of six months after the approval of Institutional Ethics Committee (IEC) Anurag University. Study population consisted of in patients from Department of Gastroenterology, Gandhi hospital, Secunderabad. Informed consent taken from patients followed by data collected from patient case sheets. Statistical analysis done using SPSS version 24. P value <0.05 and confidence interval 95% considered statistically significant. Fisher's exact test used for co-relating data. Total 100 subjects assessed in study. Majority of subjects were in age group (31-45) years 55%. A high male predominance observed of which 64% alcoholic and 36% smokers. Acute or recurrent pancreatitis (26%) followed by Diabetes mellitus (20%) were common co-morbidities observed. Ultrasound abdomen identified major calcification in 26% cases. A 6-point verbal rating scale was implemented to know patient's perception for pain severity where mild and moderate pain were 50% cases each. Tramadol was commonly used drug in 96% cases. Before and after treatment monotherapy observed to be statistically significant than other therapies (such as dual, triple, quadruple) as P value was 0.0167. Hence, appropriate selection of analgesic is vital in treatment of pain in CP.

Keywords: Pain, analgesics, chronic pancreatitis, verbal rating scale, tramadol.

Received 26.04.2025 Revised 21.06.2025 Accepted 25.07.2025

How to cite this article:
J. Rathna Deborah, P. Anusha, S. Sai Ankitha, G Naik, Divya Amaravadi, G Rajeev Kumar, P. Shravan Kumar, K Prasad Deverakonda. Efficacy of Drugs in Management of Pancreatic Pain in Chronic Pancreatitis. Adv. Biores. Special Issue [3] 2025. 59-63

INTRODUCTION

In Chronic pancreatitis (CP) the pancreas sustains damage covering more than 90% of its surface, causing pancreatic insufficiency, steatorrhea, and weight loss due to impaired exocrine function. The incidence varies with disease severity and can reach 85% in cases of severe chronic pancreatitis [1, 2] . The most common symptom that prompts patients to seek medical care is persistent or recurrent stomach pain [3]. On the other hand, pancreatogenic diabetes will eventually develop if the pancreas' endocrine function is compromised. The causes for chronic pancreatitis are known to be alcohol abuse, autoimmune diseases, genetic mutations in CFTR, PRSS1, SPINK 1 genes, ductal obstruction from tumours, stones, or trauma, hypercalcemia, hyperlipidemia causing ischemia of pancreatic tissue and organ inflammation [4]. 80%-90% patients experience pain as a typical symptom of chronic pancreatitis [5]. Pancreatic pseudocysts can cause excruciating anguish as pancreatic fibrosis progresses in chronic pancreatitis. Also current theories suggest that neuronal damage leading to peripheral sensitization and then central sensitization is essential for the emergence of chronic, usually uncontrollable pain [5,6]. It has been demonstrated that the pancreatic specific sensory neurons and dorsal root ganglia contain two distinct types of nociceptors: the transient receptor potential vanilloid 1 receptor and the proteinase-activated receptor 2 (PAR-2). Experimental models suggest that sub-inflammatory doses of trypsin could bind to the PAR-2 receptor explaining trypsin as a potential nociceptive stimulus [3]. Treatment of chronic pancreatitis involves

addressing signs, symptoms, exocrine and endocrine disorders, nutritional deficits, gastrointestinal discomfort and other physiological repercussions. Pancreatic enzymes such as lipase, amylase, and protease facilitate the digestion of fats, proteins, and starches [5]. To reduce oxidative stress vitamins and anitoxidant therapies preferred. Coeliac plexus block or bilateral thoracoscopic splanchnicectomy (BITS) procedure are primary methods for preventing neuronal transmission of pain as part of non-pharmacological therapy [7]. Coeliac plexus block is guided by endoscopic ultrasound (EUS) and CT [8]. However, analgesics are the mainstay in the pain treatment [9]. The WHO'S analgesic ladder offers a rational and consistent framework for the use of analgesic drugs such as non-opioids, strong opioids and weak opioids [10, 11]. Chronic pancreatitis has been shown to cause allodynia and hyperalgesia. Therefore, it is highly advised that people with chronic pancreatitis use antineuropathic medications like pregabalin, gabapentin, and amitriptyline [12]. Strong opioids as morphine, fentanyl, oxycodone are effective in treating chronic pancreatitis [13]. But they also possess risk of addiction in patients and so should be used only when other pain treatment options are ineffective or insufficient [14]. The major use of opioids in treating chronic pancreatitis can be observed in a study done by Kasper Grosen et al., which reported that treatment was clinically successful in 16% of cases, where the average pain intensity was reduced by at least 30% [15]. Hence, use of a multi-modal approach consisting of selection of one drug from each drug category, appropriate use of adjuncts and maximization of medical therapy are suitable in chronic pancreatitis treatment [15]. This initiated the research interest in evaluating the pain management practices followed in treating chronic pancreatitis. Further the objectives of our study included identifying the severity of pain and response to the drugs on pain before and after treatment.

MATERIAL AND METHODS

Study Design

It is prospective observational study done in the in-patient and outpatient Departments of Gandhi Hospital, Secunderabad. Study period from September'2022 to February'2023, for six months' duration. Sample Size collected was 100 cases.

Ethics committee approval

The Institutional Ethical Committee of Anurag university and Gandhi Hospital authorities examined and approved the study protocol before it started.

Study Criteria

Inclusion Criteria

- Males and females of age group 18 – 70 years of age.
- In patients from Department of Gastroenterology, Gandhi hospital, Secunderabad.

Exclusion criteria

- Paediatric age groups.
- Pregnant and lactating women.
- Patients diagnosed with chronic kidney disease, malignant conditions, congestive heart failure, pancreatic carcinoma

Study Procedure

Informed consent was taken from the patients and their informants (primary care giver) for data collection. The data collected from patient's case sheets was analyzed to evaluate the management of pain in chronic pancreatitis. To assess severity of pain in patients a 6-point verbal rating scale (VRS) was used. The patient was then asked to give his perception for pain as no pain, mild pain, moderate pain, severe pain or worst pain as per the scale pointers. Case sheets with complete information regarding patient details were included. Cases were collected on regular basis with timely follow up.

Statistical analysis

Descriptive statistics were used for data analysis. SPSS software version 24 was used for statistical analysis. The confidence interval taken was 95% and P value <0.05 was considered significant. Fisher's exact test, Chi square test, Pearson correlation tests were incorporated to draw the research results [16,17].

RESULTS AND DISCUSSION

100 patients met the study criteria were included in the study. The patient outcomes are specific to the Indian population of which 75% were male and 25% female. This was in correlation with another study done by **Deepak et al.,** which shows a higher male percentage in the study having CP [18]. Majority of the patients were in the age group of (31-45) years 55% as detailed in **Table 1.**

Table 1: Age Distribution

Age Interval (years)	n=100	Percentage
16-30	24	24
31-45	55	55
46-60	20	20
>60	01	01

This was also similar to another study done by Kavin Sugumar et al., showed 35 years as the mean age for chronic pancreatitis presentation [19]. Patients with social history of alcohol was more of 64% and smoking 36% due to which these are major risks for chronic pancreatitis. This is comparable to another study done by Gregory A. Coté et al., identified more cases of alcoholic men as the major etiology for chronic pancreatitis [20]. Another study done by J E Domínguez-Muñoz et al., demonstrates smoking and alcohol to primarily be the cause for chronic pancreatitis [21]. Vishal Sharma et al., study illustrates that after controlling for alcohol consumption, a meta-analysis of 12 studies showed that current smokers had a 2.8-fold increased relative risk of developing chronic pancreatitis compared to non-smokers. [22]. Table 2 depicts comorbidities in chronic pancreatitis consisting of maximum 26% cases of acute or recurrent pancreatitis explaining that transition to chronic pancreatitis followed by 20% diabetes mellitus cases.

Table 2: Distribution Based on Comorbidities

Comorbidity	N=100	Percentage
Hypertension	11	11
Diabetes mellitus	20	20
Cholelithiasis	02	02
Pancreatitis (Acute/Recurrent)	26	26
Gastritis	01	01
Esophageal varices	01	01
CP without any comorbidity	39	39

These findings can be linked to another done by Morihisa Hirota et al, which reports cigarette smoking to as a risk for occurrence of co morbidity such as diabetes mellitus and pancreatic calcifications [23]. Biochemical markers show elevated serum amylase levels in majority 67% patients and 55% cases with elevated serum lipase levels, in our study. Ultrasound of abdomen impression showed majority 26% cases with calcification followed by pseudocysts (11%), dilation of main pancreatic duct (11%), walled of necrosis (2%) which was similar to another study done by Kavin Sugumar reported pancreatic calcification is maximum cases of 79% [19]. The medications used in management of pain are listed in Table 3 showing 96% cases with Tramadol prescriptions used to treat pain. This is comparable to a study by Jan G D'Haese et al., which describes tramadol to be on par with stronger narcotics while having a decreased risk of addiction and gastrointestinal adverse effects [24].

Table 3: Drugs Used in Pain Management

Drug	No. of cases	Percentage
Tramadol	96	96
Tapentadol	10	10
Antoxid P (vitamins, minerals, DL methionine, selenium, yeast)	30	30
Gaba NT (Gabapentin and Nortriptyline)	22	22
Panlipase	10	10
Buscopan	30	30
Creon (pancrelipase)	01	01

30% cases prescribed each with Antoxid P given as nutritional supplement given as most patients are alcoholic which leads to nutritional deficiency. By removing any biliary sludge or microliths lodged in the sphincter of Oddi, buscopan is used to treat biliary and idiopathic pancreatitis. 22% cases prescribed with Gabapentin and Nortriptylin to treat neuropathic pain that may arise due to co-morbidities as diabetes. 10% cases prescribed with Tapentadol which is an opioid to treat severe pain and Panlipase of another 10% cases to treat pancreatic enzyme deficiency. And 1% case consisted of pancrelipase which was prescribed for pancreatic enzyme replacement therapy to aid in food digestion. These findings are in line with another study done by Larisa Umnova et al., explaining the use of pancreatic enzymes, which only impact cholecystokinin (CCK), lowers pancreatic activity and produces analgesia, and replaces exocrine function [25]. However, another study done by J E Domínguez-Muñoz reported heterogeneous

treatment modal consisting of pancreas enzyme replacement therapy (40.7 %) as the most commonly used apart from pain relieving medications [21]. Pain perception was noted by using verbal rating scale and it was observed that 50% cases were of mild pain and 50% with moderate pain. Table 4 illustrates severity of pain before treatment and after treatment on use of pain medications. Pain was observed to be reduced with monotherapy from the statistical co relation done as P value was 0.0167. However, other combination therapies were no considered statistically significant in pain management. The statistical tool used for co-relation was Fisher's exact test. Whereas another study by Larisa Umnova et al., showed the most successful treatment for patients with chronic pancreatitis was a combination of pancreatin, PPI, and NSAID [25-27].

Table 4: Treatment Outcome

Treatment (Therapy)	BT (No. of cases)		AT (No. of cases)		P value
	Mild pain	Moderate pain	No pain	Pain to be decreased	
Mono	21	08	11	18	**0.0167***
Dual	25	25	21	29	0.5475
Triple	03	14	10	07	0.2587
Quadruple	01	02	02	01	0.9999
Sextuple	0	01	01	0	0.9999

CONCLUSION

This study examined the management of pain in chronic pancreatitis among 100 patients in an Indian population. The findings revealed a higher prevalence of chronic pancreatitis in males (75%) and individuals aged 31-45 years (55%). Alcohol consumption (64%) and smoking (36%) were identified as major risk factors, aligning with previous research. Comorbidities were common, with acute or recurrent pancreatitis (26%) and diabetes mellitus (20%) being the most frequent. Pain management primarily involved the use of tramadol (96% of cases), along with nutritional supplements and other medications to address specific symptoms and complications. The study utilized a verbal rating scale to assess pain severity, with 50% of cases reporting mild pain and 50% moderate pain before treatment. Statistical analysis indicated that monotherapy was effective in reducing pain (p=0.0167), while combination therapies did not show significant improvement. These findings contribute to the understanding of chronic pancreatitis management in the Indian context.

Acknowledgement

We thank the management, staff and faculty of Anurag University for helping us in this research study and also the physicians of Gandhi Hospital for allowing us do the data collection from the cases.

Ccompeting Interest

None

Ethical Approval

The study was approved by the Institutional Review Board of Anurag university bearing the research proposal number: IRB-AGI/2022-2023/04.

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